



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/582,825

06/14/2006

Kenneth L. Arrington

21597P

8252

210 7590 04/02/2008
MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER

MOORE, SUSANNA

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

04/02/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/582,825	Applicant(s) ARRINGTON ET AL.	
	Examiner SUSANNA MOORE	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 21-24, 28, 29 and 31-34 is/are pending in the application.
- 4a) Of the above claim(s) 8-11, 21-24, 28, 29 and 31-34 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5 is/are allowed.
- 6) ☒ Claim(s) 1-4, 6 and 7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/2/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group (I) in the reply filed on 2/1/2008 is acknowledged. Applicant did not point out any errors in the restriction requirement, thus, the requirement is deemed proper and **Final**.

In summary, claims 1-7 are currently pending and under consideration. Claims 8-11, 21-24, 28,29 and 31-34 are currently withdrawn from consideration. This is a First Action on the Merits.

This application contains claims 8-11, 21-24, 28,29 and 31-34, drawn to an invention nonelected without traverse in the paper of 2/1/2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Substituted 2-Phenylthieno[2,3-d]pyrimidin-4-ones as Mitotic Kinesin Inhibitors.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1624

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites the limitation "-CH=CHO- and -CH=CHN-" in the definition of R^{4a} and R^{4b}. There is insufficient antecedent basis for this limitation in the claim.

Claims 3 and 4 recite the limitation "R⁵" in the definition of R⁶ and R⁷. There is insufficient antecedent basis for this limitation in the claim.

Claim 4 recites the limitation "(C₁-C₆)alkyl-NR⁶R⁷" in the definition of R². There is insufficient antecedent basis for this limitation in the claim.

Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of Formula 1, wherein R¹= aryl, R² is halogen, p= 1, R^{3a} and R^{3b}= hydrogen does not reasonably provide enablement for compounds of Formula 1, wherein R¹ is hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₁-C₆ perfluoroalkyl, C₁-C₆ aralkyl, C₃-C₈ cycloalkyl, and heterocyclyl, said alkyl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents

Art Unit: 1624

selected from R^4 ; R^2 is independently selected from: $(C=O)_aO_bC_1-C_{10}$ alkyl, $(C=O)_aO_b$ aryl, $(C=O)_aO_bC_2-C_{10}$ alkenyl, $(C=O)_aO_bC_2-C_{10}$ alkynyl, CO_2H , OH , $O_bC_1-C_6$ perfluoroalkyl, $(C=O)_aNR^6R^7$, CN , $(C=O)_aO_bC_3-C_8$ cycloalkyl, $(C=O)_aO_b$ heterocyclyl, $SO_2NR^6R^7$, and $SO_2C_1-C_{10}$ alkyl, said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, and heterocyclyl is optionally substituted with one or more substituents selected from R^4 ; R^{3a} and R^{3b} are independently selected from: halogen and (C_1-C_6) alkyl. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Pursuant to *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims: Scope of the compounds. Owing to the range of many variables, trillions of substituted thieno[2,3-d]pyrimidines are embraced.

Art Unit: 1624

(B) The nature of the invention: The invention is a highly substituted pyrazolo[1,5-a]pyrimidines.

(C) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(D) Direction or Guidance: That provided is very limited. Applicant shows a general synthesis of compounds of Formula 1, under Preparation on pages 18, 19 and 40 of the Specification, but does not show the starting material used to make the variety of compounds claimed. There is limited evidence in the Specification of the example compounds that only cover a small portion of the substituents claimed of Formula 1. Thus, there is no specific direction or guidance regarding said compounds of Formula 1 specifically mentioned in Scope.

The specification does not provide any support for the synthesis of compounds of Formula 1, wherein R^1 is hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_1 - C_6 perfluoroalkyl, C_1 - C_6 aralkyl, C_3 - C_8 cycloalkyl, and heterocyclyl, said alkyl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R^4 ; R^2 is independently selected from: $(C=O)_aO_bC_1$ - C_{10} alkyl, $(C=O)_aO_b$ aryl, $(C=O)_aO_bC_2$ - C_{10} alkenyl, $(C=O)_aO_bC_2$ - C_{10} alkynyl, CO_2H , OH , O_bC_1 - C_6 perfluoroalkyl, $(C=O)_aNR^6R^7$, CN , $(C=O)_aO_bC_3$ - C_8 cycloalkyl, $(C=O)_aO_b$ heterocyclyl, $SO_2NR^6R^7$, and SO_2C_1 - C_{10} alkyl, said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, and heterocyclyl is optionally substituted

Art Unit: 1624

with one or more substituents selected from R^4 ; R^{3a} and R^{3b} are independently selected from: halogen and (C_1-C_6) alkyl.

The availability of the starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 2164.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *In re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

(E) State of the Prior Art: These compounds are substituted thieno[2,3-d]pyrimidines of Formula I wherein R^1 = aryl, R^2 is halogen, $p = 1$, R^{3a} and R^{3b} = hydrogen which are well documented in the art. So far as the examiner is aware, no substituted thieno[2,3-d]pyrimidines of Formula I wherein R^1 is hydrogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_1-C_6 perfluoroalkyl, C_1-C_6 aralkyl, C_3-C_8 cycloalkyl, and heterocyclyl, said alkyl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R^4 ; R^2 is independently selected from: $(C=O)_aO_bC_1-C_{10}$ alkyl, $(C=O)_aO_b$ aryl, $(C=O)_aO_bC_2-C_{10}$ alkenyl, $(C=O)_aO_bC_2-C_{10}$ alkynyl, CO_2H , OH , $O_bC_1-C_6$ perfluoroalkyl, $(C=O)_aNR^6R^7$, CN , $(C=O)_aO_bC_3-C_8$ cycloalkyl, $(C=O)_aO_b$ heterocyclyl, $SO_2NR^6R^7$, and SO_2C_1-

Art Unit: 1624

C₁₀alkyl, said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, and heterocyclyl is optionally substituted with one or more substituents selected from R⁴; R^{3a} and R^{3b} are independently selected from: halogen and (C₁-C₆)alkyl of any kind have been made or used.

(F) Working Examples: Applicant shows example 1-4 but no working examples were shown of Formula I wherein R¹ is hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₁-C₆ perfluoroalkyl, C₁-C₆ aralkyl, C₃-C₈ cycloalkyl, and heterocyclyl, said alkyl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R⁴; R² is independently selected from: (C=O)_aO_bC₁-C₁₀ alkyl, (C=O)_aO_baryl, (C=O)_aO_bC₂-C₁₀ alkenyl, (C=O)_aO_bC₂-C₁₀ alkynyl, CO₂H, OH, O_bC₁-C₆ perfluoroalkyl, (C=O)_aNR⁶R⁷, CN, (C=O)_aO_bC₃-C₈ cycloalkyl, (C=O)_aO_bheterocyclyl, SO₂NR⁶R⁷, and SO₂C₁-C₁₀alkyl, said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, and heterocyclyl is optionally substituted with one or more substituents selected from R⁴; R^{3a} and R^{3b} are independently selected from: halogen and (C₁-C₆)alkyl were exemplified.

(G) Skill of those in the art: The ordinary artisan is highly skilled.

(H) The quantity of experimentation needed: Since there is one working example as described above, the amount of experimentation is expected to be high and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has shown lack of enablement for the groups noted

groups on Formula i. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Dugar et. al. (US 7223766 B2).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = hydrogen, R^{3b} = hydrogen, $p=1$ and R^2 = hydrogen. See column 47, line 25. Thus, claim 1 is rendered anticipated by Dugar et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by El-Baih et. al. (Journal of Saudi Chemical Society, 2000, 4(3), 281-290).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = methyl, R^{3b} = methyl, $p=1$ and R^2 = chloro or nitro. See CAS printout. Thus, claim 1 is rendered anticipated by El-Baih et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Piazza et. al. (US 6200980 B1).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = hydrogen, R^{3b} = hydrogen, $p=1$ and R^2 = 2-propoxy. See column 12, example 29, line 53. Thus, claim 1 is rendered anticipated by Piazza et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Pamukca et. al. (US 5948911 A).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = methyl, R^{3b} = hydrogen, $p=1$ and R^2 = 4-methylester. See column 29, lines 1-3. Thus, claim 1 is rendered anticipated by Pamukca et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Walter et. al. (US 6277858 B1).

The compound of formula (I), wherein R^1 = propyl, R^{3a} = bromo, R^{3b} = hydrogen, $p=1$ and R^2 = 4-bromo or 4-chloro. See column 36, compounds 3.46 and 3.47. See also column 37, compounds 3.48, 3.75, 3.76; column 38, compound 3.77; column 39, lines 3.108, 3.109 and 3.110; column 40, lines 3.133, 3.134, 3.135, 3.157, 3.158 and 3.159. Thus, claim 1 is rendered anticipated by Walter et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Oota et. al. (JP 08143571 A).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = hydrogen, R^{3b} = methyl, $p=2$ and R^2 = 2-propoxy and $NHC(O)O$ phenyl. See page 8, columns 13-14, compound 4. Furthermore, all of the compounds in the top and bottom table anticipate the reference. Thus, claim 1 is rendered anticipated by Oota et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Dumaitre et. al. (J. Med. Chem., 1996, 39(8), 1635-1644).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = hydrogen, R^{3b} = hydrogen or methyl, $p=1$ and R^2 = 2-propoxy. See page 1638, table 1, compounds 6 and 7. Thus, claim 1 is rendered anticipated by Dumaitre et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Shishoo et. al. (Indian J. Chem., 1989, 28B(12), 1039-47).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = methyl or ethyl, R^{3b} = methyl, $p=2$ and R^2 = 3,4-dimethoxy. See page 1041, compounds 26 and 28. Thus, claim 1 is rendered anticipated by Dumaitre et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Sauter et. al. (Monatshefte fuer Chemie, 1976, 107(3), 1193-7).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = hydrogen or methyl, R^{3b} = methyl, $p= 1$ and $R^2= 4$ -methoxy. See page 1194, compounds A^1 and A^2 . Thus, claim 1 is rendered anticipated by Sauter et. al.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Reid et. al. (Justus Liebigs Annalen der Chemie, 1968, 713, 143-8).

The compound of formula (I), wherein R^1 = hydrogen, R^{3a} = ethyl, R^{3b} = hydrogen, $p= 1$ and $R^2= 4$ -methyl. See CAS printout. Another compound is a compound of formula (I), wherein R^1 = hydrogen, R^{3a} = methyl, R^{3b} = methyl, $p= 1$ and $R^2= 4$ -methyl. Thus, claim 1 is rendered anticipated by Fritz et. al.

REASONS for ALLOWANCE

Claim 5 is free of the art and is enabled.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624

**/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624**